Value of EUS in early detection of pancreatic ductal adenocarcinomas in patients with intraductal papillary mucinous neoplasms

Background and study aims: Pancreatic ductal adenocarcinomas (PDAC) sometimes arise in patients with intraductal papillary mucinous neoplasms (IPMNs). This study examined the incidence of PDACs concomitant to or derived from branch duct IPMNs. The usefulness of endoscopic ultrasonography (EUS) relative to other imaging methods for detecting these tumors was also assessed.

Patients and methods: This retrospective study used data from clinical records and imaging studies that were collected prospectively. During 2001–2009, 167 consecutive patients with IPMNs underwent EUS, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). The 102 patients whose branch duct IPMNs lacked mural nodules/symptoms and thus did not qualify for resection were followed up by semiannual EUS and annual ultrasonography, CT, and MRI. The sensitivity and specificity with which the four modalities detected IPMN-derived and -concomitant PDACs at the first examination and throughout the study period were evaluated. The rate of PDAC development during follow-up was analyzed by the Kaplan–Meier method.

Results: A total of 17 IPMN-derived and 11 IPMN-concomitant PDACs were diagnosed at the first examination. Lesions that did not qualify for resection or chemotherapy were followed up for a median of 42 months. Seven IPMN-concomitant PDACs and no IPMN-derived PDACs were detected during follow-up. The 3- and 5-year rates of IPMN-concomitant PDAC development were 4.0% and 8.8%, respectively. At the first examination, EUS was superior to other imaging modalities in terms of IPMN-derived and -concomitant PDAC detection. Throughout the study period, including follow-up, EUS was significantly better at detecting IPMN-concomitant PDACs than the other modalities.

Conclusions: IPMN-concomitant PDACs are quite often found at diagnosis and during follow-up. EUS examination of the whole pancreas plays an important role in the management of IPMNs as it allows the early detection of these small invasive carcinomas.

Introduction

Intraductal papillary mucinous neoplasms (IPMN) of the pancreas develop from epithelial cells in the main pancreatic duct (MPD) or branch duct [1–4]. Histologically, these lesions can be classified into benign IPMNs (hyperplasia, adenoma, and borderline neoplasm) or malignant IPMNs (noninvasive, minimally invasive, and invasive carcinomas) [5–7]. Although the natural history of IPMNs is still poorly understood, all of these lesions are considered to be premalignant because even benign lesions such as hyperplasias or adenomas can progress to invasive carcinomas. Thus, even benign IPMNs may have to be surgically resected to prevent malignant transformation [8]. However, the risk associated with the surgical procedures should be balanced against the risk of malignant transformation [7]. Thus, to facilitate decision making it is necessary to understand the natural history of IPMNs and to identify the IPMN features that are associated with a high potential for malignancy.

The features of IPMNs usually differ from those of ordinary pancreatic ductal adenocarcinomas (PDAC) [9–11]. However, several reports have shown that relative to the incidence of PDACs in the general population, PDACs occur at higher rates in patients with IPMNs; they are also frequently discovered at an unresectable stage [12–16]. There are two types of IPMN-related PDACs, namely, those that infiltrate the IPMN (designated here as IPMN-derived PDAC) and those that are...
histologically distinct from the IPMN (designated here as IPMN-concomitant PDAC).

In recent times, it has become possible to diagnose IPMNs with a variety of imaging tools. Endoscopic ultrasonography (EUS) is superior to the other available imaging methods in terms of spatial resolution [17–20]. The present study had two main aims. The first was to investigate the natural course of branch duct IPMNs by using four imaging modalities: EUS, ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). In particular, the frequencies of cystic lesion changes and IPMN-derived and -concomitant PDAC development during follow-up were determined. The second aim was to compare the diagnostic accuracy of the four imaging modalities in terms of the detection of IPMN-derived and -concomitant PDACs.

**Patients and methods**

**Study design**

This study was approved by the Institutional Review Board of Kinki University School of Medicine. It was a retrospective study that used a database created after the clinical record and imaging examination data were collected prospectively. The surgical indications and follow-up method were unified during the study period. Outcomes were reviewed retrospectively.

**Patients**

Between April 2001 and March 2009, 167 consecutive patients who were suspected to have an IPMN had their first examinations with EUS, ultrasonography, CT, and magnetic resonance cholangiopancreatography (MRCP/MRI) at the Kinki University Hospital. All four imaging methods were performed within 1 month.

**Diagnosis of IPMNs**

With all of the imaging modalities, IPMN was defined as a dilation of the MPD or its branches. To exclude simple cysts, a lesion was suspected to be an IPMN if it was more than 5 mm in diameter. IPMN was classified from imaging studies as either main duct or branch duct IPMN according to the new Fukuoka criteria [21]. Thus, if the MPD was ≥ 6 mm, the lesion was defined as main duct IPMN. However, if the branch duct was dilated and communicated with the pancreatic duct without MPD dilation, the lesion was defined as branch duct IPMN. The lesions were also examined for the presence of mural nodules.

**Distinction between IPMN-derived and -concomitant PDACs**

IPMN-derived PDACs were distinguished from IPMN-concomitant PDACs on the basis of radiological images and macroscopic or microscopic findings of the resected specimens. A pathologist examined these specimens carefully for the presence of non-neoplastic ducts between the IPMN and PDAC: if intervening normal ducts were observed, the PDAC was defined as an IPMN-concomitant PDAC. If a histological transition between the IPMN and PDAC was observed, the PDAC was defined as an IPMN-derived PDAC [22].

**Indications for surgery and follow-up strategy**

All main duct IPMNs and the branch duct IPMNs with nodules or symptoms were surgically resected. The remaining branch duct IPMNs, which lacked nodules/symptoms, were not surgically resected; instead, the patients underwent periodic follow-up with EUS, ultrasonography, CT, and MRI as outpatients (Fig. 1). Thus, EUS was performed semiannually and the ultrasonography, CT, and MRI examinations were performed annually between the two EUS examinations: the MRI was performed 2–4 months after the first EUS examination, and both ultrasonography and CT were performed 2–4 months after the next semiannual EUS examination, after which the cycle was repeated. If one of the four modalities showed during follow-up that the cystic lesion had changed (dilation of cystic lesion ≥ 10 mm) or a nodule had appeared, the other three modalities were performed within the following month so that the detection abilities of the four modalities could be compared.

**Imaging techniques**

All imaging techniques, both at the first examination and during follow-up, were performed in a blinded manner: the endosonographers, the ultrasonographer, and the radiologists were all unaware of the results of the other imaging investigations.

**EUS**

The electronic convex echoendoscope (GF-UC240P-AL5; Olympus, Tokyo, Japan) was employed for EUS. All EUS observations of the pancreas were performed by the same two endosonographers (M.K. and H.S.), who were qualified by the Japan Gastroenterological Endoscopic Society and were experienced in EUS, having performed more than 3000 EUS examinations each.

**US**

A GE LOGIQ9 or 700 MR EXPERT Series unit (General Electric Medical Systems, Milwaukee, Wisconsin, USA) with a 2–4-MHz curved-array wide-band transducer was used for abdominal ultrasound. All ultrasound observations of the pancreas were performed by the same ultrasonographer (K.M.), who had 20 years of experience in gastrointestinal ultrasonography.

**CT**

Intravenous contrast-enhanced CT imaging was performed by using two-phase CT (Toshiba X-vigor; Toshiba Medical System, Tokyo, Japan) or a 64-channel multidetector CT scanner (Lightbox i5; General Electric Medical Systems, Milwaukee, Wisconsin, USA). CT images were obtained using two phases: arterial (50–70 seconds after the start of intravenous contrast injection) and portal venous phases (100–120 seconds after the start of intravenous contrast injection).

![Fig. 1](https://example.com/figure1.png)

**Fig. 1** The diagnostic and follow-up strategy with endosonography (EUS), ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI).
The following outcomes were calculated: (i) the frequencies of main duct IPMN, branch duct IPMNs without mural nodules/symptoms, and IPMN-derived and IPMN-concomitant PDACs at the first examination; (ii) frequencies of changes in the followed up (unresected) IPMNs and the new development of IPMN-derived and IPMN-concomitant PDACs during follow-up; (iii) the relative sensitivity and specificity with which each imaging modality detected PDAC at the first examination (to calculate these values, PDACs detected during follow-up were defined to be occult lesions that had not been detected at the first examination); and (iv) the relative sensitivity and specificity with which each imaging modality detected PDAC throughout the study period (to calculate these values, the latest examination during the study period was used). For (iv), the modality that detected the PDAC at the first examination or during follow-up was compared with the other three modalities that were performed within 1 month of the PDAC detection.

**Variables**

Statistical analysis

All analyses were performed using the statistical software SAS 9.1.3 (SAS Institute Inc., Cary, North Carolina, USA). The patients with IPMN-concomitant PDACs that were detected at the first examination were compared with the patients with new IPMN-concomitant PDACs in terms of their clinicopathological data by using Student’s t test and Fisher’s exact test. The McNemar test was applied to evaluate the differences between EUS, ultrasonography, CT, and MRI in terms of detecting PDACs. Differences were considered to be significant when \( P < 0.05 \). The development of IPMN-concomitant PDACs was analyzed by the Kaplan–Meier method.

**Results**

Clinical characteristics of patients

Table 1 shows the clinical characteristics of the 167 patients with IPMNs. The mean age was 69 years and the ratio of males to females was approximately 2:1. The IPMNs occurred twice as frequently as their pancreatic parenchymal phases (at 40 seconds) with the liver phase being obtained at 70 seconds. The images were evaluated by two radiologists (T.H. and M.K.), who had 15 and 20 years of experience in gastrointestinal radiology, respectively. The two readers first read the data independently. If either of them suspected that there was a solid tumor as well as the cystic lesions, the two readers re-assessed the images together until an agreement was obtained.

Gold standard of PDAC diagnosis

The standard for the diagnosis of PDAC was histopathology of surgically resected specimens and/or EUS-guided fine-needle aspiration (FNA) specimens plus follow-up with the four modalities every 3 months for at least 12 months (Fig. 1). In the cases where a PDAC was not suspected on the basis of the imaging studies, the final diagnoses were confirmed by follow-up (Fig. 1).

### Table 1: Clinical characteristic of the 167 patients with intraductal papillary mucinous neoplasms.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Follow-up group*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>167</td>
<td>102</td>
</tr>
<tr>
<td>Age, mean (range), years</td>
<td>69 (33–88)</td>
<td>71 (33–86)</td>
</tr>
<tr>
<td>Sex, M:F, n</td>
<td>110:57</td>
<td>61:41</td>
</tr>
<tr>
<td>Type of IPMN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main duct</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Branch duct</td>
<td>148</td>
<td>102</td>
</tr>
<tr>
<td>Site of IPMN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>114</td>
<td>64</td>
</tr>
<tr>
<td>Body/tail</td>
<td>53</td>
<td>38</td>
</tr>
</tbody>
</table>

IPMN, intraductal papillary mucinous neoplasm.

* In total, 114 of the 167 IPMN lesions were branch duct IPMNs without mural nodules or symptoms. None of these cases underwent resection and were to be followed-up by the four imaging modalities for at least 12 months. In 12 cases, this follow-up did not occur and these cases were excluded from the remaining analyses, leaving 102 cases that were followed up according to the study protocol.
because follow-up was no longer possible due to the occurrence of other serious diseases, namely, gastric cancers (n=4), colon cancers (n=2), and benign diseases (n=37). The median duration of follow-up was 42 months (range 12–122).

Outcomes of imaging examinations during follow-up period
In 3 of the 102 followed-up patients, the diameter of the dilated branch ducts increased during follow-up (Fig. 2). In all cases, all four imaging modalities detected this change. All three patients underwent surgical resection, but the histological diagnoses of the surgical specimens revealed that they had intraductal papillary mucinous adenomas (IPMAs). Mural nodules did not develop in any of the followed-up branch duct IPMNs. Thus, new IPMN-derived carcinomas did not arise from the branch duct IPMNs themselves during follow-up. However, seven (7%) IPMN-concomitant PDACs were detected in the follow-up period between 12 and 74 months after the initial diagnosis of IPMN (Figs. 3, 4). Thus, the 3- and 5-year rates of IPMN-concomitant PDAC development were 4.0% (95%CI 0.1–7.9) and 8.8% (95%CI 1.2–16.4), respectively. All lesions were detected at an operable stage, but one patient rejected surgical resection because of his advanced age and underwent chemotherapy instead.

Outcomes of surgical resection and histopathological examinations
Over the course of the study, surgery was performed in 58 patients because the IPMN was accompanied by a concomitant PDAC (n=13), the IPMN was a main duct IPMN or a branch duct IPMN with mural nodules/symptoms (i.e. the IPMN met the IPMN surgical resection indications, n=42), or the cystic lesion became enlarged during the follow-up period (n=3). Pathological analysis of the resected lesions revealed that all had been correctly diagnosed as IPMNs by the preoperative studies. In the 17 IPMN-derived PDACs detected at the first examination, all of which were resected immediately, histology revealed clear interconnections between the PDAC and the IPMN. Of the 18 IPMN-concomitant PDACs that were detected at the first examination or during follow-up, 13 were resected and histology revealed that all of these IPMNs were clearly divided from the PDAC by normal pancreatic duct.

Characteristics of patients with IPMN-concomitant PDACs
Table 2 summarizes the clinicopathological features of the 11 patients with IPMN-concomitant PDACs that were detected at the first examination and the seven patients with IPMN-concomitant PDACs that were detected during follow-up. Whereas two-thirds of the IPMNs of all of these cases were located in the pancreatic head, the PDACs showed the opposite orientation, with
two-thirds or more detected in the body or tail. This tendency was particularly pronounced in the seven PDACs discovered during follow-up: six were located in the body or tail. All concomitant IPMNs were branch duct IPMNs without mural nodules. The concomitant PDACs that were detected at the first examination had a mean (±SD) size of 24 ± 10.6 mm. By contrast, the concomitant PDACs of the follow-up group were smaller (16 ± 7.5 mm), although this difference did not achieve statistical significance (P = 0.085). In the seven patients whose PDACs were detected during follow-up, the longest diameter of the dilated branch duct and the width of the pancreatic duct at the first examination were 13 ± 3 mm and 4 ± 1 mm, respectively. These duct dimensions did not increase during follow-up.

**Sensitivity and specificity of imaging modalities to detect IPMN-derived and -concomitant PDACs**

Table 3 summarizes the sensitivity and specificity with which the four modalities diagnosed IPMN-derived and -concomitant PDACs at the first examination and throughout the study period. For the calculations regarding the first examination, the seven IPMN-concomitant PDACs that were discovered during follow-up were considered to be occult lesions that had not been detected by any of the imaging modalities at the first examination. At the first examinations, EUS seemed to be superior to the other imaging modalities in detecting both IPMN-derived and -concomitant PDACs, although only the difference between EUS and ultrasonography achieved statistical significance. During follow-up, six of seven new PDACs were first detected by EUS despite the fact that ultrasonography, CT, and MRI had been performed between 2 and 10 months earlier (Fig. 4). The other three modalities were then performed within 1 month of the PDAC-detecting EUS. For IPMN-concomitant PDAC that was detected during follow-up, EUS, ultrasonography, CT, and MRI detected 100% (7/7), 0% (0/7), 43% (3/7), and 43% (3/7), respectively. Thus, EUS was still superior to ultrasonography, CT, and MRI in detecting these PDACs. When calculating sensitivity and specificity of the four modalities to detect IPMN-concomitant PDACs at the latest examination throughout the study period including follow-up, EUS was significantly better than the other three imaging modalities (Table 3).

The other three modalities were then performed within 1 month of the PDAC-detecting EUS. For IPMN-concomitant PDAC that was detected during follow-up, EUS, ultrasonography, CT, and MRI detected 100% (7/7), 0% (0/7), 43% (3/7), and 43% (3/7), respectively. Thus, EUS was still superior to ultrasonography, CT, and MRI in detecting these PDACs. When calculating sensitivity and specificity of the four modalities to detect IPMN-concomitant PDACs at the latest examination throughout the study period including follow-up, EUS was significantly better than the other three imaging modalities. (Table 3).

**Table 3** Sensitivity and specificity with which endosonography, ultrasonography, computed tomography, and magnetic resonance imaging detected intraductal papillary mucinous neoplasm-derived and -concomitant pancreatic ductal adenocarcinoma.

<table>
<thead>
<tr>
<th>Modality</th>
<th>IPMN-derived PDACs (n = 17)</th>
<th>IPMN-concomitant PDACs (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At the first examination</td>
<td>Throughout the study period</td>
</tr>
<tr>
<td></td>
<td>Sensitivity, % [95% CI]</td>
<td>Specificity, % [95% CI]</td>
</tr>
<tr>
<td>EUS</td>
<td>100 [0.83–1.00]</td>
<td>85 [0.83–0.85]</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>47 [0.31–0.55]</td>
<td>99 [0.97–1.00]</td>
</tr>
<tr>
<td>CT</td>
<td>53 [0.35–0.66]</td>
<td>97 [0.95–0.99]</td>
</tr>
<tr>
<td>MRI</td>
<td>53 [0.35–0.71]</td>
<td>92 [0.90–0.94]</td>
</tr>
</tbody>
</table>

CI: confidence interval; CT: computed tomography; EUS: endosonography; IPMN: intraductal papillary mucinous neoplasm; MRI: magnetic resonance imaging; PDAC: pancreatic ductal adenocarcinoma.

During follow-up, IPMN-derived PDACs were not detected, but IPMN-concomitant PDACs were detected in seven patients. When comparing the imaging methods at the first examination, the seven PDACs that were detected during follow-up were considered to be occult lesions that had not been detected by any of the imaging modalities. When comparing the imaging methods throughout the study period, the latest examination during study period was used.

* McNemar test
Discussion

When IPMN lesions are examined by imaging, it is necessary to check for mural nodules and to determine whether the lesion communicates with the MPD. EUS has better spatial resolution than ultrasonography and CT and can therefore more clearly visualize the internal structure of cystic tumors of the pancreas [20]. For this reason, EUS is often used to follow-up IPMNs in order to assess whether changes in the cystic lesions have occurred. In the present study, EUS was also useful for detecting IPMN-concomitant PDACs both at the first examination and during follow-up.

IPMN is a cystic tumor that has a marked potential to progress to a malignant state. Several studies indicate that 60%–100% of resected main duct IPMNs are malignant [4, 23–26]. Therefore, in patients with good life expectancy, main duct IPMNs should be resected. By contrast, branch duct IPMNs are associated with a lower risk of malignancy [4, 23–26]. However, the 2012 international consensus guidelines recommend that branch duct IPMNs that have a higher likelihood of malignancy should be surgically resected. Predictors of malignancy in these IPMNs are the presence of large branch ducts (>30, 35, 40 or 50 mm) and a particular height of mural nodules (>5 or 10 mm) [25, 27–30]. However, the natural history of branch duct IPMNs is poorly understood. In the present study, all branch duct IPMNs with mural nodules and/or symptoms were resected regardless of the dilated branch duct and mural nodule size, whereas the patients with branch duct IPMNs without mural nodules or symptoms were followed up by EUS (and other imaging modalities) to check the IPMN growth and to judge whether the patients with these IPMNs should undergo surgery. Although mural nodules never arose during follow-up, the cystic lesions in three (3%) patients grew in size during follow-up and were resected. Histology revealed that all three were IPMAs. Thus, IPMN-derived carcinomas were not detected during follow-up in the present study. These observations are consistent with an increasing body of evidence that suggests that most branch duct IPMNs can be followed up [4, 26–31]. For example, when Salvia et al. prospectively evaluated the effectiveness of follow-up for a median of 32 months in 89 asymptomatic patients with branch duct IPMNs (>3.5 cm) without mural nodules, only five (5.6%) exhibited an increase in lesion size and were resected [26]. Histological examination of those resected specimens revealed that none were malignant. Another prospective study found that in 69 of 82 patients (84.1%) with branch duct IPMNs without mural nodules, the lesions did not change during a median follow-up period of 61 months [31]. These reports suggest that branch duct IPMNs without mural nodules rarely progress to cancer over short periods of follow-up. Nevertheless, more follow-up data are needed to improve our understanding of the natural history of branch duct IPMNs without mural nodules.

In the present study, 11 IPMN-concomitant PDACs (7% of all IPMNs) were incidentally detected by several imaging methods at the first examination for IPMNs. Several studies have also shown that IPMNs are frequently accompanied by carcinomas that are distinct from IPMNs, both at the first medical examination and during IPMN follow-up [12, 15, 16]. Uehara et al. [15] reported that the 5-year rate of ductal carcinoma development in 60 patients with branch duct IPMNs was 6.9%, and Tada et al. [16] reported that 5% of patients with IPMN developed PDAC during a 3.8-year follow-up. Similarly, Yamaguchi et al. [22] showed that 4.1% of patients diagnosed with IPMN also had an IPMN-derived or -concomitant PDAC. The 5-year rate of IPMN-concomitant PDAC in the present study was 8.8%, which is higher than the rates of the latter studies, although it should be noted that the studies differed in terms of median follow-up period and cohort size. The higher rate in the present study may relate to the strict periodic follow-up with several modalities and the fact that EUS was used. These factors may have been responsible for the detection of the other seven PDACs during follow-up, which increased the 5-year rate.

The use of EUS together with the periodic follow-up probably also allowed the detection of these seven PDACs at an early stage. These PDACs may be indolent and thus would not have manifested as clinical cases had they been left in place. Uehara et al. reported that the IPMN-concomitant PDACs that were detected during follow-up, largely by transabdominal ultrasonography, were found in an advanced state, even though the patients were examined at 6-month intervals [15]. By contrast, in the present study, all of the PDACs that were detected during follow-up could still be resected. During follow-up, six of the seven IPMN-concomitant PDACs were first detected by EUS despite the fact that ultrasonography, CT, and MRI had been performed between 2 and 10 months earlier.

The utility of EUS for the follow-up of IPMNs is also indicated by the fact that, when comparing the four modalities after one modality detected a PDAC, EUS detected all of these seven PDACs, whereas CT and MRI only detected 43% of these lesions and ultrasonography could not detect any. Accordingly, EUS detected PDACs significantly better than the other modalities throughout the study period including follow-up. Thus, EUS appears to be more useful than ultrasonography, CT, and MRI for the early detection of PDACs. However, it should be noted that there was some methodological bias because EUS was performed semiannually whereas the other modalities were only performed once per year. This may have increased the sensitivity of EUS. However, although it would have been preferable to follow the patients up with all four modalities during the same visit, this was not done because it would have placed an undue burden on the patients.

To our knowledge, this study is the first to employ EUS for the follow-up of branch duct IPMNs. This observation suggests that, in cases of partial surgical resection, the in situ gland should be subjected to close surveillance. This approach would also aid the early detection of PDACs. Moreover, considering the malignant potential of the in situ gland, total pancreatectomy may be indicated in some cases of IPMN. However, in these cases, the complications associated with total pancreatectomy, such as diabetes and indigestion, should be balanced against the risk of malignant transformation. Moreover, Yamaguchi et al. have reported that IPMN-concomitant PDACs are significantly smaller, less invasive, and less extensive than ordinary PDACs [22]. These factors should be considered when deciding the extent of resection particularly in elderly patients. The relatively high frequency of IPMN-associated PDACs also indicates that it is important to carefully survey the entire pancreas in patients with an IPMN rather than focusing only on the cysts, as this allows concomitant carcinoma to be detected. Moreover, unresected IPMNs should be subjected to periodic follow-up with EUS to ensure that IPMN-concomitant PDACs are detected early, although the optimal interval between follow-up examinations of branch type IPMNs is not yet clear.

A recent report from Japan that analyzed radiological images and macroscopic or microscopic findings showed clearly for the first time that some PDACs exist concomitantly with IPMNs rather
IPMNs without mural nodules, concomitant carcinomas will appear during follow-up: the present study showed 3- and 5-year rates of IPMN-concomitant PDAC development of 4.0% and 8.8%, respectively. Performing EUS at regular follow-up visits will help to detect these new carcinomas early. Moreover, it may be necessary to consider resecting branch duct IPMNs without mural nodules although this option should be balanced against surgical complications.

**Competing interests:** None

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**References**


than deriving from them [22]. By contrast, several reports on IPMNs in Western countries [26, 32–34] did not report cases of such concomitant PDACs. This discrepancy may reflect the fact that such IPMN-concomitant PDACs were not sought in the latter studies. Alternatively, or in addition, it may also reflect differences between races in terms of PDAC pathogenesis. In conclusion, when diagnosing and treating IPMNs, it is necessary to search for concomitant carcinomas, as the present study showed that 7% of these lesions were accompanied by carcinomas elsewhere in the pancreas. EUS is expected to play the prominent role in detecting these carcinomas at IPMN diagnosis. Moreover, in a substantial proportion of cases with branch duct